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症　　例

Cerebral Mucormycosis

---Report of a Case---

by

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Recently the fungus infection tends to be on the increase with relation to the therapy of antibiotics, steroids, or antimetabolic agents[10)21)]. Above all the infections due to Aspergillus, Candida, Cryptococcus, Actinomycetes or Nocardia are clinically seen. Species of genera Mucor, Rhizopus, Absidia, Mortierella and Basidiobolus, all of a class Phycomycetes, have been known to be ubiquitous molds in nature, and have not been ordinarily considered as pathogens. But these fungi may rarely encroach on a superficial mucous membrane of the nose, paranasal sinuses, respiratory tracts or alimentary canals. Ultimate diagnosis should be based on histological demonstration of the characteristic nonseptate hyphae invading tissues. It is said that mucormycosis of the orbit and central nervous system is generally caused by species of Mucor, Rhizopus or Absidia[5)].

Mucormycosis is a rare disease especially in the central nervous system[8)11)14)24)26)]. Since PALTAUF[19)] reported the first authentic case of lung in 1885, nearly 153 cases were collected from the literatures[7)23)] up to 1962. Total cases have been about 160 to 1967[20)]. One-third of these cases involves the central nervous system, orbits, nasal and paranasal sinuses. The infection is usually a complication of other diseases, of which diabetes is the most common. Other predisposing diseases are blood disorders, tuberculosis and generalized malignancies.

The following case we experienced is no complication with diabetes mellitus, but characteristic nonseptate hyphae were histologically demonstrated from intracranial granulomatous tumor excised by right temporal craniotomy.

CASE REPORT

History. T. K., a 54 year-old woman who recongnized right hemicrania with pain of right eye at the end of March, 1966. Simultaneously the visual acuity became poor, palpebra ptotic, and finally the right eye resulted in blindness at the middle of April. She was once admitted and examined in our Clinic on June, but obvious intracranial abnormalities could not be obtained from cerebral angiograms.

Although the eye symtoms and hemicrania did not change, the patient was discharged on August 5, 1966. After that the pain on right hemicranium and on right eye continued more than a year from the onset of troubles. She was again admitted to our Clinic on

June 13, 1967. Other days prior the second admission she underwent the operations twice under diagnosis of glaucoma, but her troubles did not at all reduce.

Examination. The patient was right-handed woman. Consciousness was always clear. Roentgenograms of chest and physical examinations revealed no disorders. Plain skull film suggested only slight inflammation of right ethmoid sinus. Blood pressure was normal. The cerebrospinal fluid pressure was found to be 200 mmH_2O by lumbar puncture. Cerebrospinal fluid showed the increase of protein (100 mg/dl) without xanthochromia. Integrated findings of cerebrospinal fluid were given as follows :

Examination of cerebrospinal fluid

Protein	100 mg/dl	Initial pressure	200 mmH_2O (-5ml)
Sugar	88 mg/dl	Terminal pressure	140 mmH_2O
Chloride	416 mg/dl	Cell count	73/3

Tryptophane reaction : negative QUECKENSTEDT's phenomenon : normal

Colloidal gold test : 0001111000

Leucocyte count in peripheral blood was 11500 per cubic millimeter. Some neutrophils had DOEHLE's inclusion bodies and heavy granules. Erythrocyte count was 314×10^4 per cubic millimeter. Blood sugar was 95 mg/dl. WASSERMAN reaction was negative, and Spermine reaction positive. Slight hepatic dysfunction was found due to the systematic examination of blood. Left hearing loss was verified by audiogram. Electroencephalogram disclosed the slight slowing in right hemisphere. Intraocular tension was normal. Visual acuity was completely lost on right eye, and also fairly poor on opposite side (0.4). There was hypesthesia in the divisions of the trigeminal nerve on right half of face

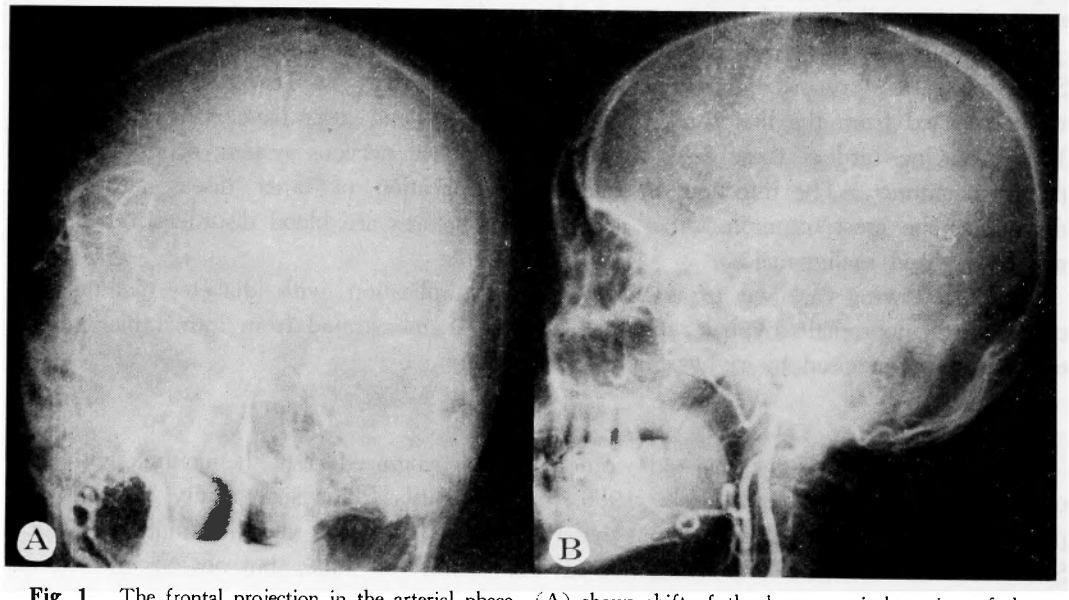

Fig. 1. The frontal projection in the arterial phase (A) shows shift of the lower vertical portion of the anterior cerbral artery and marked elevation of the horizontal portion of the middle cerbral artery. However, there is no medial displacement of the vessels over the outer surface of the island of Reil. The lateral view (B) reveals elongation of carotid siphon and elevation of the anterior half branches of the middle cerebral artery. Filling of the anterior cerebral artery is poor.

and right parietal area. The mass lesion within middle fossa was confirmed by means of right carotid angiography as shown in Fig. 1 and 2.

Operation : On June 19, right fronto-temporal craniotomy was done under general anesthesia. In anterior portion of middle fossa the brown-colored thumb- sized granulomatous mass was found to be intracerebral, so it was excised as much as possible.

Microscopic Examination : It was found to be cerebral mucormycosis for the first time by microscopic findings of tumor. Microsections of the extirpated tissues revealed the sporadic necrotic lesions with neutrophilic infiltrations surrounding them and massive proliferation of broad nonseptate branching hyphae (Fig. 3)

Postoperative clinical course : Although consciousness was clear after operation, the remarkable improvement of right eye ailments such as pain, ptosis, numbness around eye and visual acuity, could not be at all obtained. But any complications due to operation did not occur. On July 14 electroencephalogram was recorded, but this showed the slowing on right hemisphere as before. Despite of the cultures of fungi from paranasal discharges and cerebral spinal fluid in several times, fungi could not be demonstrated. Cerebrospinal fluid pressure increased up to 370 mmH_2O and revealed whitish turbid colour on August 1. Cell count was 3200/3 in which a majority of cells were segmented nuclear. Consciousness was yet no doubt clear as usual.

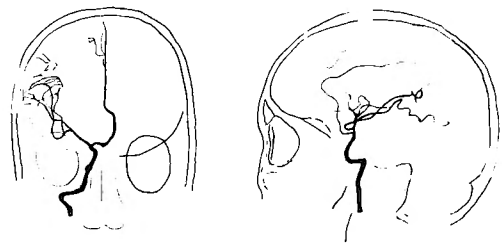

Fig. 2. Sketches represent the gross appearance that was noted in the preceding figures.

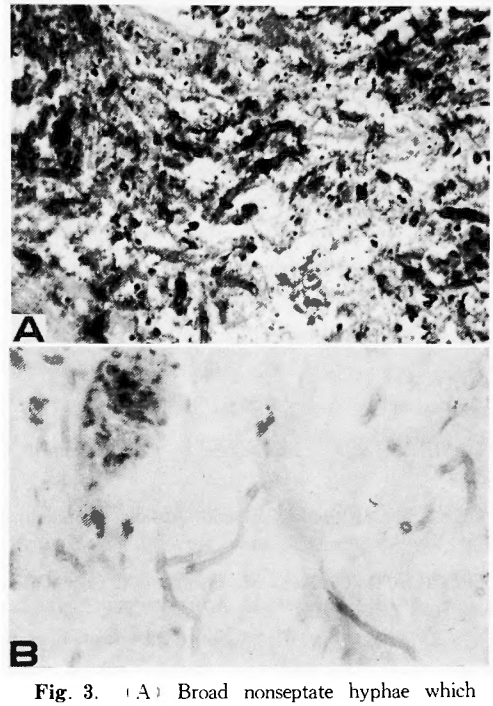

Fig. 3. (A) Broad nonseptate hyphae which stain fairly clear with hematoxylin-eosin are demonstrable. Hither and thither neutrophilic cellular infiltrations are also seen (×400)
(B) PAS stain

Since then appeared the turbid cornea on right side. The examination of right optic fundus showed the bleeding around the disc, and it denoted a picture of neuritis optica.

Before long on August 6 she became suddenly deeply comatose, and the respiration irregular, unstable and frequently short disruption.

Immediately the endotracheal intubation was indicated and the artificial respiration due to automatic mechanism maintained her life for six days. But she could not rise from the death. As the family did not permit to perform the post mortem examination, the details of pathological evidence to death could not be confirmed.

DISCUSSION

Although the infection with saprophytic fungi of the class Phycomycetes has been reported in nearly 160 patients, only eight have survived[20]. The infection in humans is characterized by proliferation in tissue of broad, nonseptate branching hyphae rarely septate.

There has been some confusion in nomenclature concerned with this infection. The first human infection described was assigned to the genus mucor, hence, the name mucormycosis. Later Rhizopus and Absidia were shown to be etiologic agents, but the name mucormycosis was remained because the involved fungi all belonged to the family mucoraceae (Fig. 4). But Lie et al[13] insisted that the term "phycomycosis" should be used as it could be widely applied for the infections with Basidiobolus and a member of another phycomycetous orders.

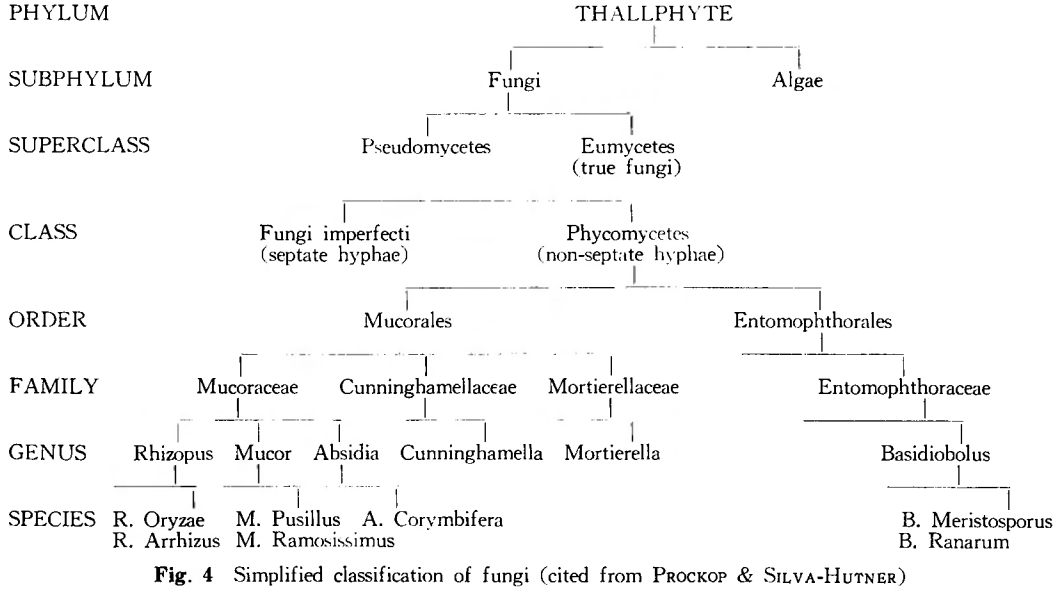

Fig. 4 Simplified classification of fungi (cited from PROCKOP & SILVA-HUTNER)

The molds, by preference, invade blood vessels causing thrombus formation (mucor thrombosis) and infarction of surrounding tissues. The head, neck, lungs, and gastrointestinal tract are most frequently involved. The fungus causes sinusitis, thrombosis of the retinal artery, complete ophthalmoplegia and blindness. Generally the disease occurs in patients who have debilitating disease, or who have received antibiotics, steroids, or antitumor agents, and is particularly prone to develop in patients with diabetic acidosis[16]. PROCKOP et al reported that, of all infections with the class Phycomycetes, forty-two percent were diabetic. According to BAUER et al[2] six in eleven cases of cerebral mucormycosis have occurred in acidotic patients, and BAKER[1] found diabetes mellitus of seven in thirteen cases. Further spread may cause meningitis or involvement of the ophthalmic, carotid and cerebral arteries. It is described in the majority of reports that most cases of cerebral mucormycosis run a rapid fulminating fatal course.

The clinical features of cerebral mucormycosis, however, have not received sufficient attention. When infections spread to the brain along to blood vessels or following the

thrombosis, the patients mostly reveal the symptoms resembling to brain tumor, brain abscess or brain softening. Localizing in paranasal or orbits, and not involving the central nervous system, the infection is possibly curable by adequate treatments[9].

Although it is referable that the fungi are isolated from the patient such as the case reported by BAUER, cultural isolation of such saprophytic organisms is not always necessary in diagnosis LE COMPTE et al[12] mentioned in 1947 that whenever the inflammation of the orbits or meningoencephalitis is complicated in the patient of severe diabetes mellitus, cerebral mucormycosis ought to be first suspected. The disease, therefore, should be kept in mind whenever a ketotic diabetic patient with sinusitis complains of facial pain, or there are neurological abnormalities which may include ptosis, limitation of ocular movement and trigeminal anesthesia. SMITH and KIRCHNER[22] have emphasized the diagnotsic value of the presence of a black turbinates in nasal mucormycosis. Anyhow, final diagnosis depends upon histological demonstration of the characteristic hyphae invading tissues. Biopsy of accessible lesions would also decide conclusive evidence.

From the therapeutic point of view early diagnosis is imperative. Early treatment for diabetic acidosis and any accompanying illness is essential. Mycostatin[17][18], Amphotericin B[3][4][16][18][25], Griseofulvin[6] and other fungal antibiotics have been used but not yet received sufficient evaluation. Bacterial antibiotics and ACTH or adrenocorticosteroids should be avoided, or used only with extreme caution. Amphotericin B is generally considered to be indicative. Use of heparin or other anticoagulants might be taken into consideration, because the mucors so often spread along or within the intima of blood vessels, and make the thrombosis and infarction. But when paradoxical thrombosis[15] occur in patient, who have severe hemorrhagic tendency, heparin therapy would be questionable.

On the other hand, the surgical treatment is all in excision of the infected tissues and debridement of all devitalized structures. Removal of the necrotic tissues would not only eliminate the infection but would facilitate control, if present, for the acidotic state.

As for prognosis, mucormycosis is an extremely serious disease regardless of the region affected. Especially in the case of disseminated or cerebral mucormycosis its prognosis is by far more serious than in any other isolated lesion. Therefore this has been generally considered a fulminating disease with a relative short course, while, in some cases, there is histopathologic evidence of subacute, or chronic inflammation. In short, the duration and severity of mucormycosis may vary from an overwhelming infection of a few days' duration to a chronic disorder that may persist for months or, in rare cases, years.

SUMMARY

A case of cerebral mucormycosis was reported of a 54 year-old woman without definite diabetes mellitus. Histopathological findings of tissues excised from right intracranial middle fossa revealed massive proliferation of characteristic nonseptate hyphae invading tissues. At 49th day after operation the patient ran suddenly a rapid fulminating fatal course. The detailed detection could not be gotten post mortem. The direct cause of death was possibly considered the bleeding out of infected vascular vessels. Some problems concerned with diagnosis and treatment were also discussed.

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和文抄録

脳ムコール菌症の1例

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藻菌類（Phycomycetes）に属する真菌が中枢神経系を侵した症例を経験したので報告した．患者は54才の女で入院1年3ヵ月前頃から右偏頭痛及び右眼の疼痛をきたすようになり，視力も漸次減退して来た．当科入院迄2回にわたつて緑内障の診断のもとに手術をうけているが愁訴は全く改善されなかつた．入院時は右眼筋麻痺と右眼の失明を認め，右顔半分の知覚鈍麻を証明した．糖尿病，血液疾患や結核等を思わす所見はなかつた．右頸動脈撮影で右中頭蓋窩の space-occupying lesion が確認されたので右側頭開頭術を施行した．硬膜を切開し中頭蓋窩前縁内側寄りに母指頭大の肉芽腫性腫瘤を認めたので出来るだけ剔出した．組織学的には所々に壊死性変化が見られ好中球を主とした細胞浸潤と特徴的な巾の広い隔壁をもたない菌糸が多数認められ，藻菌類による真菌性肉芽腫であることが判明した．術後は頭痛や右眼の愁訴の改善をほとんど見なかつたが，その他の neurological deficits は全くなく順調に経過していたが，術後49日目に急に意識障害が現われ，その1週間後に死亡するという電撃的な経過を辿つた．剖検所見は得られなかつた．